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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The purpose of this work is to develop and validate molecular biomarkers found in blood, tissues, or other bodily fluids, which may be used for the early detection of lung cancer among military personnel and veterans. Over the course of the sixth year of this award, we have made significant progress towards enrollment in both clinical trials, including the addition of two new recruitment sites. We have recruited ~75% of the 500 total subjects in the indeterminate pulmonary nodule study (Protocol 1), and ~60% of the 800 total subjects in the longitudinal screening study (Protocol 2). We have also added a junior faculty pulmonary physician and scientific program manager to supplement the leadership of this project. Additionally, the Leadership, Steering, Adjudication, Biostatistics, Imaging and Biomarker Committees continue to meet regularly. Most notably, significant progress has been made in adjudication of cases and controls within DECAMP1 which will facilitate the validation of our cancer biomarkers. We have also made significant progress towards discovering novel molecular biomarkers for lung cancer detection in the endobronchial biopsy and nasal brushing samples. Finally, we continue to identify additional funding sources to both supplement infrastructure support within DECAMP and pursue additional biomarker studies.

15. SUBJECT TERMS Nothing listed

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Table of Contents

Introduction:

The purpose of this work is to develop and validate molecular biomarkers that may be used for the early detection of lung cancer. By recruiting approximately 500 patients with indeterminate pulmonary nodules from Military Treatment Facilities and Veteran's Administration Hospitals, DECAMP plans to identify 75 patients with lung cancer for our molecular studies. For the study to develop tests that can identify the patients at highest risk for having or developing lung cancer, DECAMP will recruit approximately 800 high-risk current and former smokers from these same hospitals, determine whether they have lung cancer now and then follow them annually for up to four years to determine if they develop lung cancer. We expect to identify 50 patients who did not have cancer when they join the study, but develop lung cancer while they are being monitored. The clinical applications of this study will come from the development of tests to more accurately diagnose disease at an early potentially curable stage but also predict the occurrence of lung cancer in the future. Additionally, these biomarkers found in blood, other body fluids, or tissues will be collected more easily and are less invasive than surgery. Non-invasive collection of biological samples will be less painful for the patient and allow easier and more frequent monitoring of disease. The intent of this research is to develop early detection strategies that will ultimately decrease lung cancer deaths. This will improve the health and welfare of the military, and the American public as a whole.

Body:

During the sixth year of the DECAMP consortium, we have made significant progress toward the Specific Aims of the grant. Specifically, recruitment of subjects into both clinical trials has continued to progress (see Tables 1-4 for cumulative and yearly accrual by site, for DECAMP-1 and -2; see Figures 1-4 for cumulative and yearly accrual by month, for DECAMP-1 and -2). As would be expected in a multicenter trial, these tables demonstrate that there is heterogeneous recruitment between the sites. Cumulatively, 375 subjects have now been enrolled in DECAMP-1, and 472 subjects in DECAMP-2. Demographic information on these subjects is shown in Tables 7-8. The RA team continues to meet biweekly to discuss recruitment, including any changes or revisions to sample collection or inclusion criteria, and to share patient recruitment and screening strategies.

With an increasing number of subjects being recruited, one challenge within the consortium is ensuring high quality clinical data collection. Sites are tasked with providing necessary and appropriate documentation for each subject to support the clinical diagnosis declared by the site. This may prove to be quite challenging, as the wrong document may be uploaded, information may be entered incorrectly, and clinical diagnoses are not always certain. To rectify this situation, Boston University has added a junior faculty pulmonary physician who will focus on reviewing and overseeing all clinical data entry, and will be responsible for ensuring that the necessary and appropriate documentation is obtained for all subjects enrolled in the study. An additional challenge is the coordination of the multiple, parallel scientific projects within the consortium. While individual sites and site PIs have ownership over specific scientific aims including imaging, molecular biomarkers and protein biomarkers, integration of these findings will be crucial for evaluating the utility of these findings and in creating a comprehensive tool for lung cancer early detection. Identifying an individual to oversee all scientific aims and goals of this study is therefore an important step in the evolution of the consortium. To this end, Boston University has added a Scientific Program Manager who, in addition to coordination the consortium, will be responsible for accelerating the scientific deliverables.

Along with our progress towards patient enrollment, we have continued to evaluate the data and biospecimens collected from the clinical sites. Currently, there are a total of 19,708 samples on 665 subjects banked at the Biorepository of Boston University and there are additional samples pending shipment from individual sites (Tables 10 and 11). In addition, a total of 1,384 tissue specimens on 482 subjects are currently banked at MD Anderson and have been reviewed by consortium pathologists (Table 13). In this reporting period, we completed a complete inventory and review of these samples, and the histology of the reviewed biopsies are shown in Table 14. Of the evaluated biopsies, the majority are normal epithelium (349/561 in DECAMP 1 and 404/692 in DECAMP 2), in addition to many denuded epithelium, basal cell hyperplasia, squamous metaplasia, mild dysplasia and moderate dysplasia samples. Additionally, we continue to process and sequence samples for our biomarker work, including bronchial brushings (n=360), nasal brushings (n=130) and bronchial biopsies (n=73). For these samples we also have continued to evaluate the quality and quantity of RNA isolated, for each site (Table 9). In those sites with lower yields and poor quality, we provided feedback and reviewed the protocol for sample collection. Finally, our team has also made significant strides in quality control of the images submitted to DECAMP (Tables 5-6), and continues to track site compliance with image submission. Over the past 12 months, in those sites with low imaging compliance, we have

provided feedback to ensure that they continue to submit CT images in a timely fashion. In all, collection of this data is stored is tracked and stored in our clinical database, and the current database is summarized in Table 12.

One of the major milestones achieved over the past 12 months is the adjudication of 289 total cases and controls in DECAMP-1, an additional 189 subjects from previous years. Of these 289 subjects, 185 have been confirmed to have a lung cancer diagnosis, 97 as benign samples and 7 as metastatic cancer. As adjudicated case numbers have been a limiting factor in moving forward with our biomarker validation studies, this is a significant step for the biomarker progress within DECAMP. In the seventh year, the biomarker committee will review our current biomarkers and select candidates for a second phase of validation, on the newly adjudicated cases and controls. In addition, our sixth year of the DECAMP consortium also saw the addition of two new recruitment sites, at Boston University Medical Center, and the University of California Los Angeles. The addition of these sites presents an opportunity for increasing our enrollment numbers, and in the last 3 months we have already recruited 7 patients at BUMC into DECAMP-1.

In addition, we have made significant progress towards our scientific discovery aims. Prior work from BU has identified alterations in bronchial and nasal epithelial cell gene-expression associated with lung cancer. Using specimens from DECAMP-1 (50 lung cancer patients and 34 benign), we have sought to evaluate the ability of nasal epithelial gene-expression to identify patients with lung cancer among ever smokers with indeterminate pulmonary nodules. We identified 37 differentially expressed genes from the nasal epithelium associated with lung cancer status (FDR $q<0.05$), and concordant enrichment of the nasal signature was observed by Gene Set Enrichment Analysis in patients with indeterminate pulmonary nodules from a screening cohort at Lahey Hospital Medical Center (19 lung cancer patients and 19 benign). Additional samples will be profiled in year 7 in order to build a biomarker for early detection of lung cancer in high-risk smokers with indeterminate pulmonary nodules. Second, we have leveraged the unique collection of bronchial biopsies from DECAMP-1 in order to identify differences in gene expression pathways between smokers with and without lung cancer. Given that airway biopsies contain a mixture of lung cell types, these samples provide an unprecedented opportunity to characterize both the airway immune and epithelial responses in smokers who develop lung cancer. We found that the airway transcriptome in subjects with lung cancer is altered compared to subjects with benign nodules (20 patients with malignant nodules, 18 benign; 22 genes differentially expressed with cancer status, FDR $q<0.25$). Down-regulated genes in cancer subjects were strongly associated with functions of the immune response and a decrease in airway leukocyte content, suggesting that the immune microenvironment of the airway "field of injury" may be altered among ever smokers who develop lung cancer.

We have also made major progress in securing additional funding for the DECAMP consortium. We have successfully negotiated an additional two-year contract with Janssen Pharmaceuticals to support the lung cancer imaging and gene expression biomarkers in DECAMP-1. In addition to Janssen, we have also initiated a partnership with Novartis, as part of a four-year contract to support gene expression and protein biomarkers in DECAMP-2. Finally, the consortium will play a significant role in the recently funded Stand Up to Cancer Lung Cancer Interception Dream Team, with Dr. Avrum Spira as the principal investigator on this proposal. DECAMP will

serve as a crucial cohort in this study, providing an opportunity to develop novel imaging, ctDNA and single-cell nasal gene-expression biomarkers for lung cancer detection.

Additional accomplishments in the past 12 months are included in the summary of our progress related to each of the tasks in our SOW as specifically outlined below.

Task 1 Clinical Trial Accrual

Project 1 – Accrual Target 500 total subjects: Within that cohort, we will match lung cancers/controls for the biomarker studies
Biospecimen collection: blood, endobronchial biopsies, nasal brushings, bronchial brushings, buccal scrapings, sputum, urine
Current Accrual: See Tables 1-2 and Figures 1-2

Project 2 – Accrual Target 800 total subjects: Within that cohort, we will match lung cancers/controls for the biomarker studies
Biospecimen collection: blood, endobronchial biopsies, nasal brushings, bronchial brushings, buccal scrapings, sputum, urine
Current Accrual: See Tables 3-4 and Figures 3-4

1a. Clinical site Accrual: Based on accrual rates, the projected accrual over the 18 month No-Cost Extension is outlined in the graph below. In order to maintain or exceed these rates, the Coordinating Center will work closely with each site to reach these goals using goal-setting, recruitment tactics, and screening logs to maximize

Site	DECAMP-1	DECAMP-2
Boston VA	25	29
Boston University Medical Center*	30	0
Dallas VA	7	2
Denver VA	4	16
LA VA/UCLA*	9	38
Nashville VA Medical Center	7	20
Philadelphia VA/UPenn	30	5
Pittsburgh VA	7	0
Roswell Park Cancer Center	0	4
Brooke Army Medical Center	3	0
Naval Medical Center Portsmouth	9	23
Naval Medical Center San Diego	18	38
Walter Reed National Military Medical Center	27	56
Total	**182**	**231**

**Note that funding for patient recruitment at BUMC and UCLA is provided by the NIH/NCI.*

1b. Samples collected:

Biosamples	Quantity	Analytes	Project 1 Diagnostic	Project 2 Screening
Blood*	50 mL	Protein/RNA/DNA	Plasma Protein	-------
Blood*	50 mL	RNA	Exosomal miRNA	-------
Endobronchial Biopsies via Bronchoscopy	6 biopsies**	Protein/RNA/DNA	-------	-------
Endobronchial Brushings via Bronhcoscopy	1 brush	RNA	23 Gene Expression Marker	-------
	1 brush	Protein	-------	-------
	1 brush	DNA	-------	-------
Nasal Brushings	2 brushes	RNA	-------	Gene expression profiling
Buccal Scrapings	1 brush	RNA	-------	-------
Sputum	-------	DNA	-------	-------
Urine	25 mL	Metabolomics	4 Metabolite Marker	-------
Tumor Tissue***	-------	DNA/RNA	-------	-------

* **Plasma, Serum, PAXGene, Streck**

** **2 biopsies are obtained from three subsegmental carinas (RUL, LUL, RML)**

*** **Paraffin and fresh frozen tissue where available**

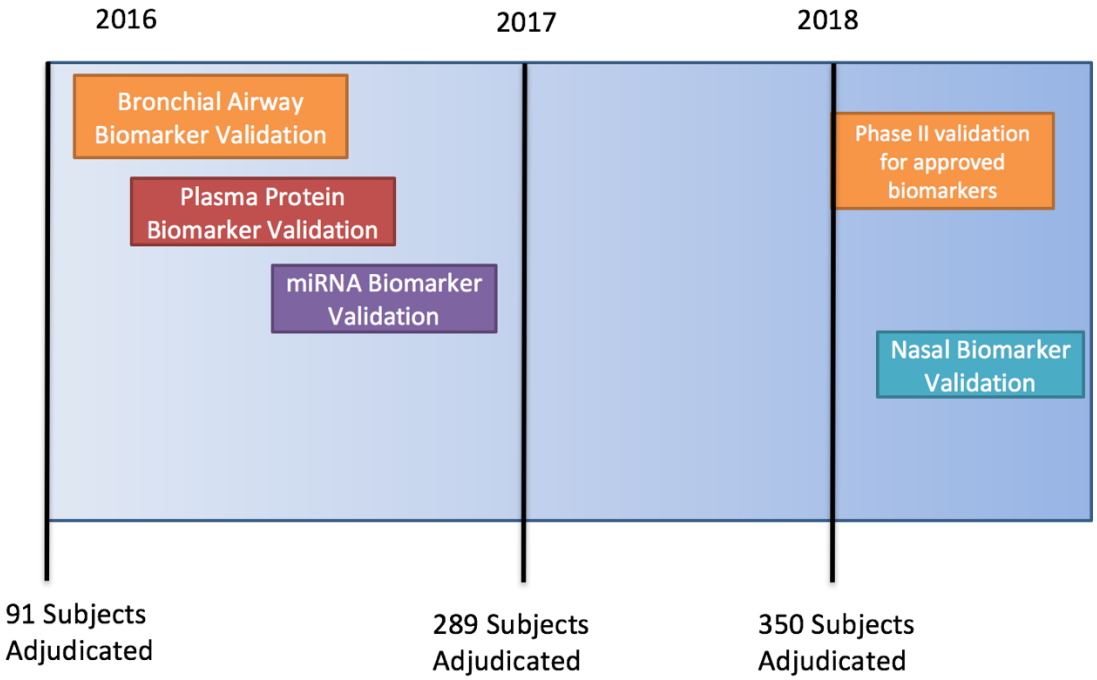
1c. Core Labs

- **Biorepository:** The Biorepository Core will continue to receive, store, and track all biospecimens in the DECAMP Consortium. Ms. Spencer will provide Dr. Moses with a spreadsheet, updated quarterly, of all specimens being housed in and pulled from the Biorepository Core at BU.
  Ms. Spencer continues to provide a spreadsheet, updated monthly. Please see Table 11 for updated sample numbers.
- **Pathology:** The Pathology Core at MD Anderson will continue to store all ambient samples provided by clinical sites of bronchial biopsy and surgical tissue. MD Anderson will also continue to process formalin-fixed samples.
  MD Anderson continues to provide a spreadsheet, updated monthly. Please see Table 13 for updated sample numbers.
- **Biostatistics:** The Biostatistics Core at Brown University will continue to

maintain the database and provide support for biomarker analysis.
The Biostatistics Core at Brown holds biweekly biomarker analysis meetings to update progress on biomarker analysis and manuscript writing.

Task 2 Biomarkers

2a Validation



- Bronchial Airway gene-expression Biomarker: We have successfully validated a 23 gene airway biomarker in 91 DECAMP-1 subjects to date from (phase 1). We plan to validate this biomarker under the direction of the biomarker committee in an additional set of ~100 subjects from DECAMP-1 in Winter 2017/Early 2018 (phase 2).
  The results of the phase 1 bronchial airway gene-expression biomarker validation were presented at the July 2017 EAB meeting. During FY6 we have made significant progress in adjudication in support of a phase 2 validation.
- Plasma Protein Biomarker: We have attempted to validate three protein markers in the serum of the same 91 subjects: C4d , CRP and CYFRA21. We will re-evaluate the utility of a phase 2 validation under the direction of the biomarker committee in Winter 2017/Early 2018.
  The results of the phase 1 plasma protein biomarker validation were presented at the July 2017 EAB meeting. During FY6 we have made significant progress in adjudication in support of a phase 2 validation.
- Plasma miRNA Biomarker: We have attempted to validate ten microRNAs generated from a discovery set in DECAMP-1, in the blood of the same 91 subjects utilized in previous phase 1 biomarkers. We will re-evaluate the utility of a phase 2 validation under the direction of the biomarker committee in Winter 2017/2018.

The results of the phase 1 plasma miRNA biomarker validation were presented at the July 2017 EAB meeting. During FY6 we have made significant progress in adjudication in support of a phase 2 validation.

2b Biomarker Discovery

We have sequenced mRNA from the nasal epithelium of 84 subjects in DECAMP-1 to refine an existing nasal gene-expression biomarker for lung cancer diagnosis in Spring 2017. We will also sequence additional nasal epithelium samples from ~100 subjects from DECAMP-1 to evaluate a potential biomarker of risk in Winter 2017/Spring 2018.

Nasal epithelium samples from 100 DECAMP-1 subjects are currently being RNA-sequenced at Walter Reed.

Task 3 DECAMP Committees

- Leadership Committee: meets monthly; continues to meet monthly
- Steering Committee: meets monthly; continues to meet monthly
- Adjudication Committee: meets as needed; continuous adjudication being processed; currently 289 subjects adjudicated. The committee will meet again in December 2017
- Biomarker Committee: meets as needed depending on when biomarkers are being proposed; the committee continues to meet as needed, most recently in June 2017 to discuss adjudication and determine a process for selecting biomarkers for phase 2 validation
- Biostatistics Committee: meets biweekly; led by the Biostatistics core at Brown. Continues to meet biweekly
- Imaging Working Group: meets monthly; led by Dr. Denise Aberle and Dr. Caroline Chiles. Continues to meet monthly
- Publication Committee: begins official meetings once first draft of first paper is completed; a first draft of a protocol paper is currently being edited by members of the leadership committee. Completion of the draft will trigger the first publication committee meeting, projected for early 2018
- Data Access Committee: meets as needed; led by ACRIN.

DECAMP-1 (ACRIN 4703)

Table 1: DECAMP 1 Cumulative Accrual by Submitting Institution

Cumulative Accrual Yr 1 through Yr 6 (Jan 2013 – Sept 2017)
nt Accrual by Every Submitting Institution : 4703

ACRIN	
Walter Reed National Military Medical Center	65
VA Boston Healthcare System	57
Naval Medical Center San Diego	50
Phila/Veterans Administration Hosp	38
Brooke Army Medical Center	35
Hospital of the University of Pennsylvania	30
VA Greater Los Angeles Health Care System	23
Nashville VA Medical Center	19
Naval Medical Center - Portsmouth	18
Dallas VA Medical Center	15
VA Pittsburgh Healthcare System	12
Boston University School of Medicine	7
VA Eastern Colorado Health Care System	6
TOTAL :	**375**
GRAND TOTAL :	**375**

Figure 1: DECAMP 1 Cumulative Accrual: January 2013 - September 2017

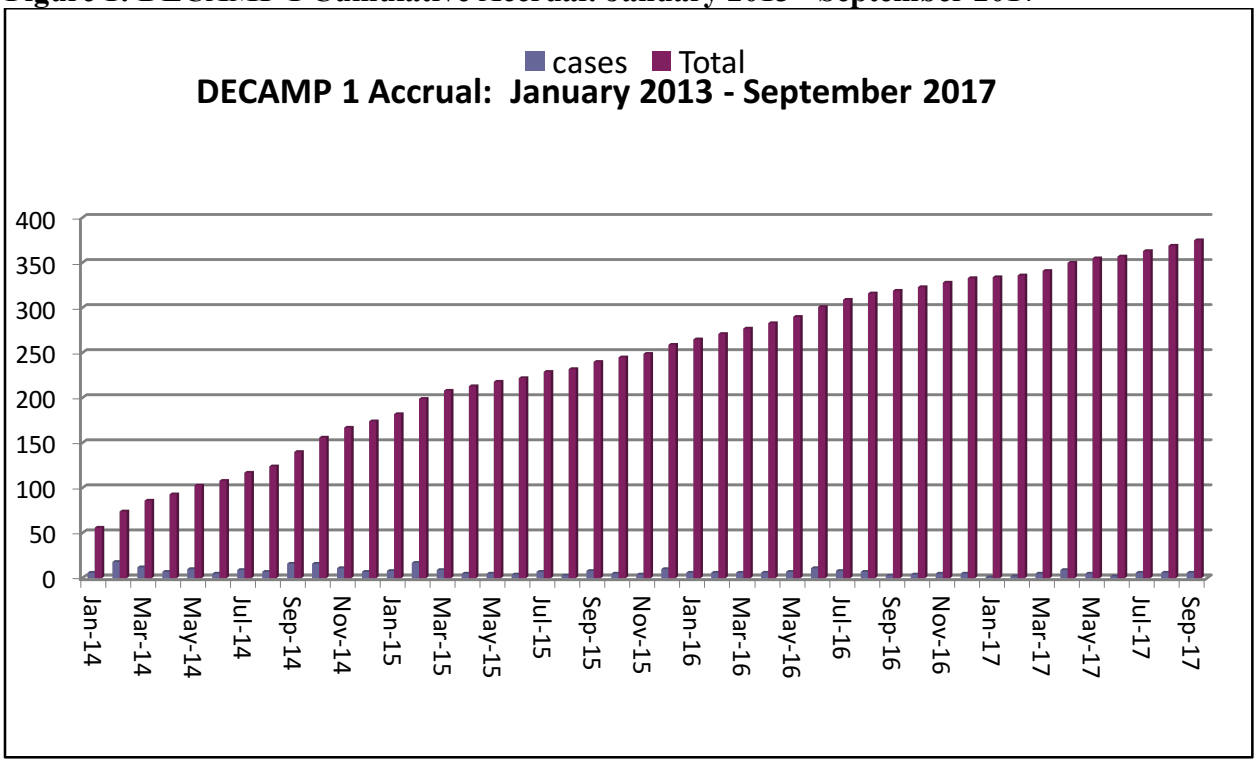


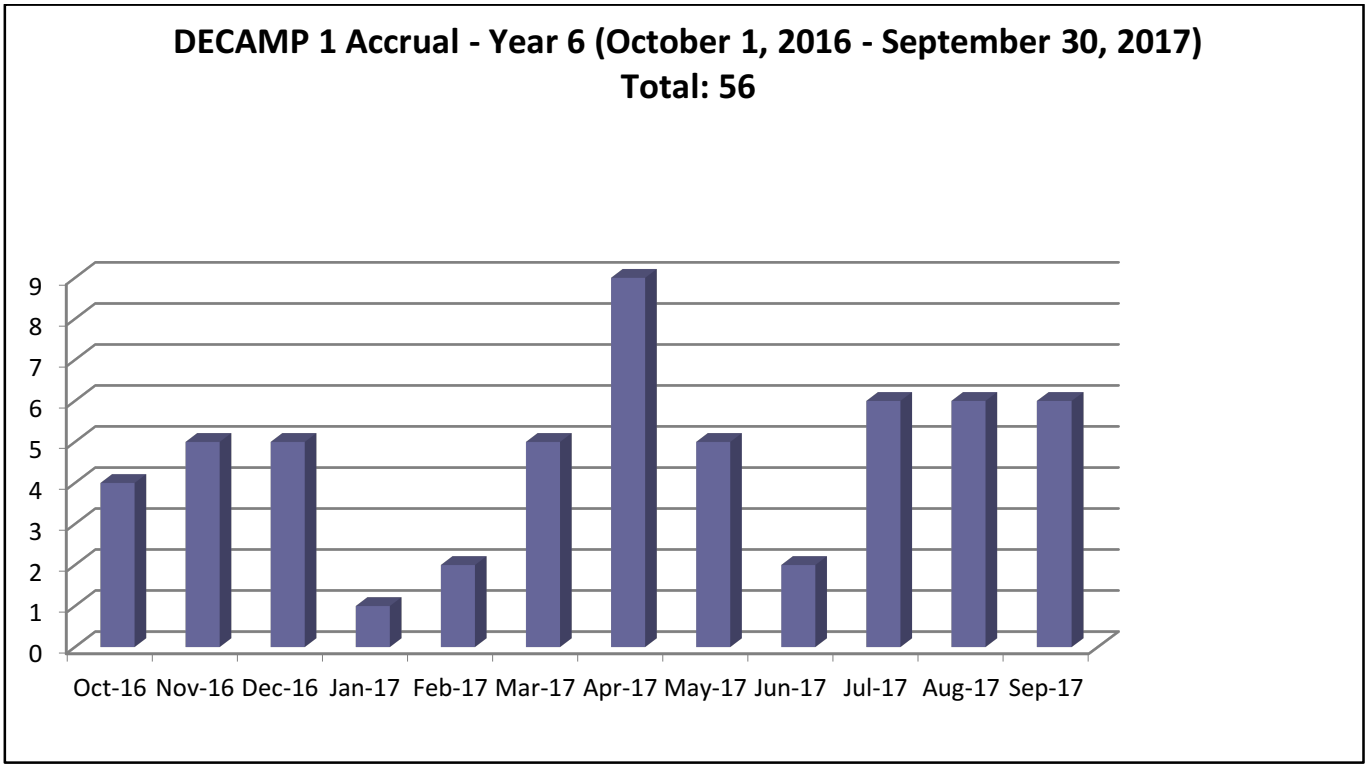
Table 2: DECAMP 1 Accrual Year 6 (Oct 2016 – Sept 2017)

DECAMP 1 Accrual Year 6 (Oct 2016 – Sept 2017)

Patient Accrual by Every Submitting Institution : 4703

ACRIN	
Naval Medical Center San Diego	15
Phila/Veterans Administration Hosp	9
VA Boston Healthcare System	7
Boston University School of Medicine	7
Nashville VA Medical Center	6
Walter Reed National Military Medical Center	5
VA Greater Los Angeles Health Care System	5
Dallas VA Medical Center	1
Hospital of the University of Pennsylvania	1
TOTAL :	**56**
GRAND TOTAL :	**56**

Figure 2: DECAMP 1 Accrual Year 6 (Oct 2016 – Sept 2017)



DECAMP 2 (ACRIN 4704)

Table 3: DECAMP 2 Cumulative Accrual

Cumulative Accrual Yr 2 through Yr 6 (Nov 2013 – Sept 2017)

Cumulative Accrual Yr 2 through Yr 6 (Nov 2013 – Sept 2017)
tient Accrual by Every Submitting Institution : 4704

ACRIN	
Walter Reed National Military Medical Center	100
Naval Medical Center San Diego	97
VA Greater Los Angeles Health Care System	81
VA Boston Healthcare System	47
VA Eastern Colorado Health Care System	46
Naval Medical Center - Portsmouth	40
Nashville VA Medical Center	39
Brooke Army Medical Center	9
Hospital of the University of Pennsylvania	7
Roswell Park Memorial Institute	4
Dallas VA Medical Center	1
VA Pittsburgh Healthcare System	1
TOTAL :	472
GRAND TOTAL :	472

Figure 3: DECAMP 2 Cumulative Accrual: November 2013 - September 2017

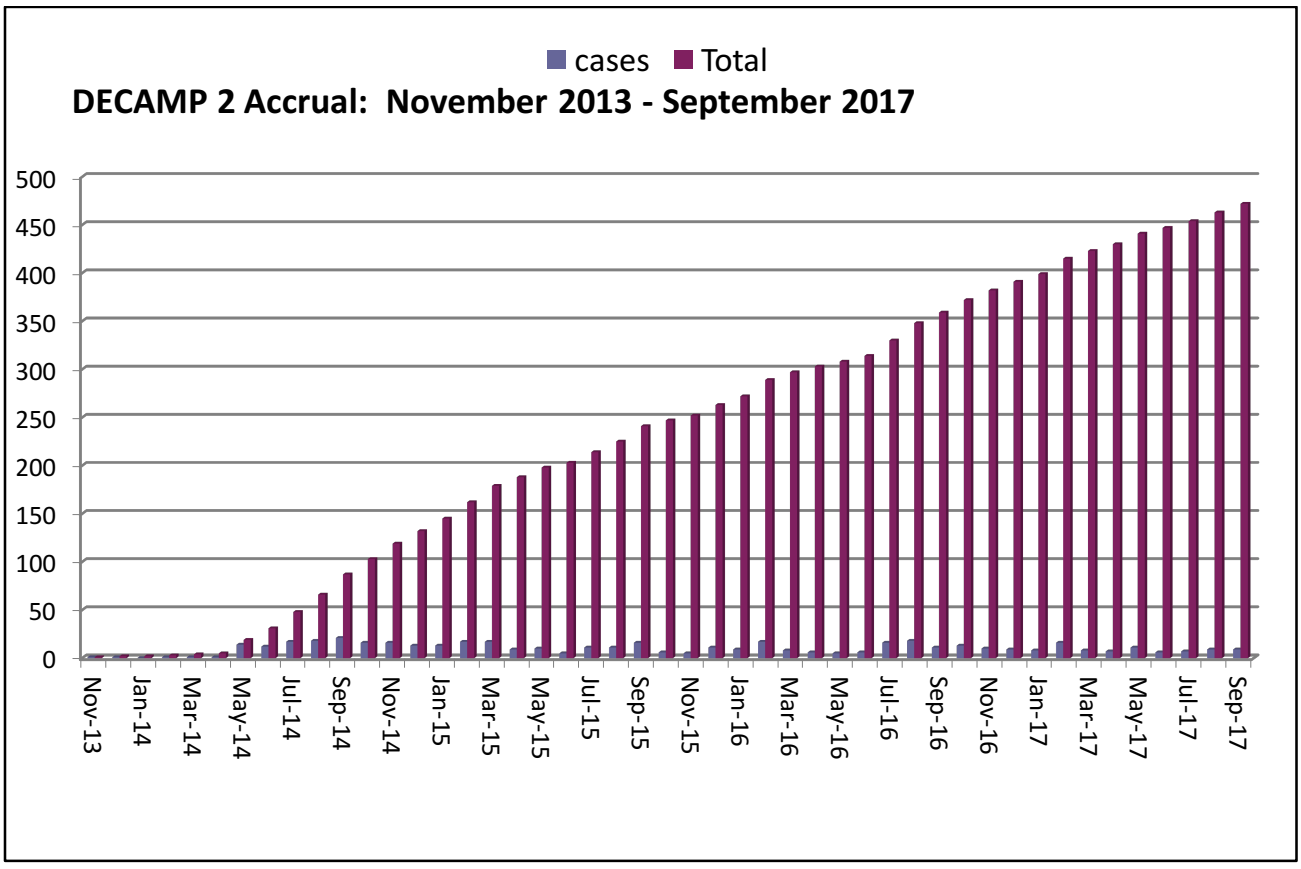


Table 4: DECAMP 2 Accrual Year 6 (Oct 2016 – Sept 2017)

Accrual Year 6 (Oct 2016 – Sept 2017)

Patient Accrual by Every Submitting Institution : 4704

ACRIN	
Naval Medical Center San Diego	37
VA Eastern Colorado Health Care System	18
VA Greater Los Angeles Health Care System	16
VA Boston Healthcare System	15
Walter Reed National Military Medical Center	14
Naval Medical Center - Portsmouth	7
Nashville VA Medical Center	5
VA Pittsburgh Healthcare System	1
TOTAL :	**113**
GRAND TOTAL :	**113**

Figure 4: DECAMP-2 Accrual: Year 6 (Oct 2016 – Sept 2017)

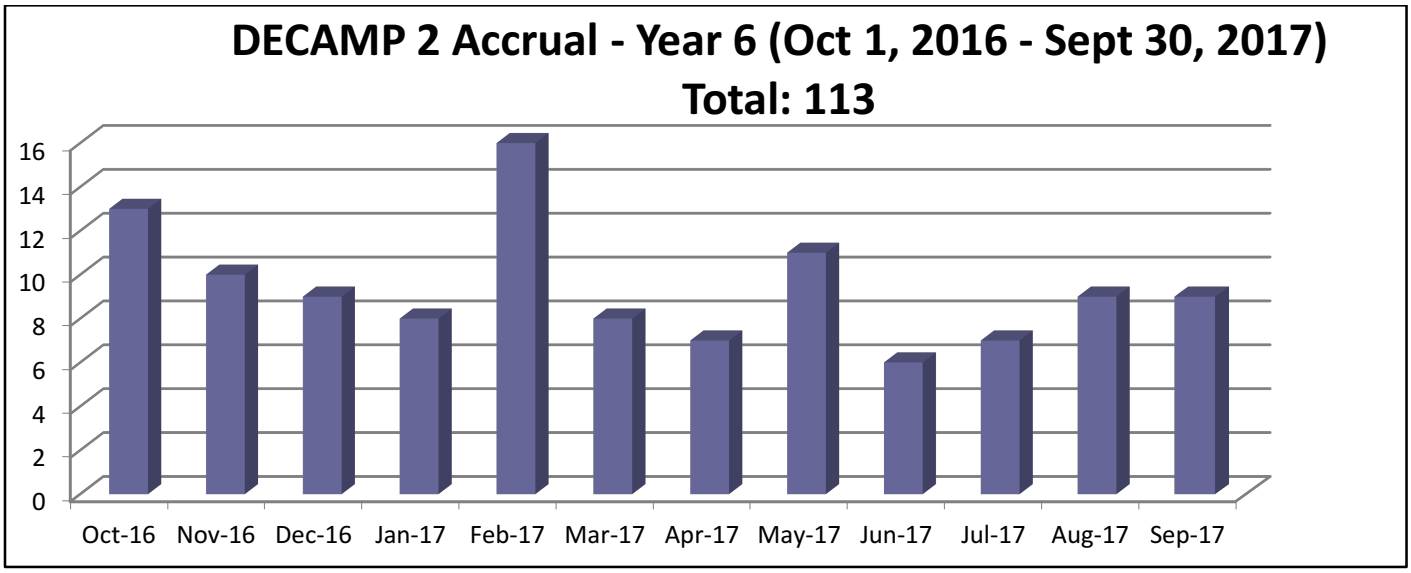


Table 5: DECAMP-1 Imaging QC

	Site	Submitted	QC'd	Baseline Exams	Follow-Up Exams
4202	Hospital of the University of Penn	27	27	26	1
4238	Brooke Army Medical Center	37	37	35	2
4278	Roswell Park Cancer Institute	0	0	0	0
4438	VA Los Angeles Healthcare	25	24	22	2
4714	VA Philadelphia	30	29	27	2
4790	VA Boston Healthcare	69	69	58	11
4791	VA North Texas Healthcare	17	17	13	4
4792	VA Eastern Colorado	11	11	6	5
4793	VA Nashville Medical Center	21	20	17	3
4794	VA Pittsburgh Healthcare	53	53	12	41
4795	Walter Reed National Military MC	61	61	54	7
4796	Naval Medical Center San Diego	104	104	51	53
4797	Naval Medical Center Portsmouth	36	36	18	18
4798	Boston Medical Center	4	1	1	0
Total		**495**	**489**	**340**	**149**

Table 6: DECAMP-2 Imaging QC

	Site	Submitted	QC'd	Baseline Exams	Follow-Up Exams
4202	Hospital of the University of Penn	12	12	7	5
4238	Brooke Army Medical Center	10	10	8	2
4278	Roswell Park Cancer Institute	9	8	3	5
4438	VA Los Angeles Healthcare	113	113	64	49
4790	VA Boston Healthcare	81	81	48	33
4791	VA North Texas Healthcare	1	1	1	0
4792	VA Eastern Colorado	58	58	38	20
4793	VA Nashville Medical Center	76	76	38	38
4794	VA Pittsburgh Healthcare	1	1	1	0
4795	Walter Reed National Military MC	68	63	60	3
4796	Naval Medical Center San Diego	156	156	90	66
4797	Naval Medical Center Portsmouth	64	64	34	30
Total		**649**	**643**	**392**	**251**

Table 7: DECAMP-1 Table 1

Demographic information for DECAMP-1 (n=375)		
Nodule Size	Mean	1.5
	Range	0.7-3.0
Age	Mean	68
	Range	47-89
Gender	Female	84
	Male	291
Race	White	272
	Black	64
	Asian	9
	Other	7
	Not Reported/Unknown	23
Smoking Status*	Current	140
	Former	163
Pack Year	Mean	52.1
	Range	20-185
COPD**	Yes	152
	No	164
FEV1%***	Mean	74.9

*Missing data on 72 subjects

**Missing data on 59 subjects

***Missing data on 58 subjects

Table 8: DECAMP-2 Table 1

Demographic information for DECAMP-2 (n=467)		
Age	Mean	63.8
	Range	50-79
Gender	Female	96
	Male	371
Race	White	342
	Black	84
	Asian	14
	Other	10
	Multiple Races	3
	Not Reported/Unknown	14
Smoking Status	Current	184
	Former	283
Pack Year*	Mean	44.3
	Range	2.1-160
COPD**	Yes	223
	No	174
FEV1%**	Mean	70.3

*Missing data on 41 subjects

**Missing data on 70 subjects

Table 9: Biosample Quality and Quantity

Site	Nasal							Bronch Brush							Bronch Biopsy						
	Sample Count	RIN			Yield (ug)			Sample Count	RIN			Yield (ug)			Sample Count	RIN			Yield (ug)		
		Avg	Min	Max	Avg	Min	Max		Avg	Min	Max	Avg	Min	Max		Avg	Min	Max	Avg	Min	Max
4202	12	3.8	2.3	7.1	4.58	0.02	15.3	23	6.70	3.7	8.6	4.07	0.73	13.62	10	5.9	2.4	8.6	0.99	0.06	2.43
4238	9	3.9	2.5	10	0.83	0.16	3.56	25	6.51	2.3	9.2	1.73	0.25	4.19	0						
4278	0							3	5.93	3.1	8.2	2.97	1.19	6.04	0						
4438	14	5.2	2.5	8.1	2.15	0.41	4.77	36	6.55	2.1	8.6	1.32	0.16	4.72	10	5.3	2.7	8.2	0.72	0.21	1.43
4714	4	3.4	2.6	4.6	7.07	1.6	15.51	9	6.47	2.7	9.1	4.39	2.06	8.31	4	2.9	2.2	4.5	0.88	0.46	1.29
4790	30	4.7	2.0	8.3	3.38	0.19	11.01	54	7.12	3.5	9.2	3.30	0.36	10.36	13	5.8	1.1	8.6	1.45	0.19	2.97
4791	6	3.3	2.5	5.8	0.38	0.24	0.54	5	5.10	2.6	6.9	2.30	0.07	4.54	3	4.9	2.5	6.7	1.38	1.09	1.94
4792	3	6.2	4.9	7.2	7.98	1.5	14.35	5	7.98	7.2	8.9	3.97	1.01	7.07	3	3.1	2.9	3.4	2.07	0.65	4.09
4793	4	4.0	2.5	7.1	0.66	0.14	1.101	16	5.73	2.2	7.7	2.60	0.55	5.18	4	2.6	2.2	2.8	1.30	0.71	2.77
4794	2	4.0	3.3	4.7	3.52	1.93	5.121	2	7.30	6.6	8.0	4.37	4.34	4.39	3	3.5	2.6	5.2	0.62	0.06	1.31
4795	19	5.2	1.7	9.0	8.54	0.75	22.87	78	6.47	2.3	9.4	2.53	0.24	15.36	7	5.7	2.4	9.1	0.68	0.25	1.07
4796	15	3.9	2.0	6.5	2.15	0.69	4.892	91	6.48	2.5	8.8	2.44	0.18	7.64	8	3.4	2.3	6.4	0.57	0.20	1.12
4797	12	3.8	2.0	7.1	1.89	0.26	7.138	13	6.42	4.2	8.6	2.86	1.01	6.84	8	3.7	2.4	7.8	0.86	0.17	2.15
All Sites	**130**	**4.4**	**1.7**	**10**	**3.66**	**0.02**	**22.87**	**360**	**6.56**	**2.1**	**9.4**	**2.64**	**0.07**	**15.36**	**73**	**4.7**	**1.1**	**9.1**	**1**	**0.06**	**4.09**

Table 10: Percentage of Subjects (by Site) with at Least One Sample

Site ID Number	Plasma	Serum	PAXgene	Urine	Buccal	Nasal	Bronch	Biopsy (68)	Biopsy (70)	Biopsy (72)	Sputum
4202	100%	100%	97%	29%	89%	94%	97%	86%	86%	77%	0%
4238	95%	100%	97%	95%	32%	32%	95%	0%	0%	3%	11%
4278	75%	75%	75%	75%	75%	75%	75%	50%	50%	75%	75%
4438	96%	96%	96%	91%	96%	93%	84%	84%	84%	83%	30%
4714	96%	96%	96%	28%	80%	96%	96%	68%	68%	52%	0%
4790	97%	96%	96%	96%	97%	99%	95%	86%	86%	82%	73%
4791	69%	69%	63%	56%	75%	88%	94%	88%	88%	88%	38%
4792	94%	94%	94%	79%	91%	91%	94%	94%	94%	94%	52%
4793	84%	81%	84%	86%	81%	81%	65%	51%	51%	53%	60%
4794	92%	92%	8%	81%	88%	85%	92%	85%	85%	81%	69%
4795	77%	78%	72%	64%	83%	86%	86%	80%	80%	73%	51%
4796	96%	96%	95%	92%	96%	97%	94%	89%	89%	84%	40%
4797	71%	73%	67%	75%	69%	73%	69%	57%	57%	57%	69%

Table 11: Sample Collection Across All Sites

	Plasma	Serum	PAXgene	Urine	Buccal	Nasal	Bronch	Biopsy (68)	Biopsy (70)	Biopsy (72)	Sputum
N (Subjects with at least one sample)	594	597	562	521	566	579	583	508	501	477	301
Total Subjects	665	665	665	665	665	665	665	665	665	665	665
% Subjects with Sample	89%	90%	85%	78%	85%	87%	88%	76%	75%	72%	45%
Total Number of Cryovials	4164	4130	1377	3579	706	1360	2096	598	621	625	452

Total of all Cryovials: 19,708

Table 12: DATA COLLECTION as of Oct 17 2017

Current Database Build Stats

	# of Unique Folders (Timepoints)	# Unique Forms	# Unique Fields	# of Automatic Validations Programmed	# Updates to DB (since activation of trial)
DECAMP 1	24	91	1153	1448	24
DECAMP 2	35	104	1510	1498	13

Case Status

	Number Enrolled	On Study	Removed Prior to Completion	Completed per Protocol
DECAMP 1	375	204	43	128
DECAMP 2	469	404	65	0

Data Collection

Overall	Total # of Cases	Total Number of Forms Entered	Total Number of Fields Entered	# Queries
DECAMP 1	375	19,049	710,557	27013
DECAMP 2	469	28,028	1,239,952	30087

	DECAMP 1	DECAMP 2
# of Forms Expected	21051	37848
% Overdue	2.35%	15.09%

Data Collection- # of Cases

	DECAMP 1	DECAMP 2 Baseline	DECAMP 2 Year 1	DECAMP 2 Year 2
PFT	353	425	261	128
Bronchoscopy	349	399	N/A	126
CT Image	353	432	259	136
Blood	363	408	348	221

Table 13: Total Cases/Specimens Received by Pathology Core

	Cases Received	Cases Reviewed	Total Specimens
DECAMP-1	242	242	631
DECAMP-2	240	240	753
TOTAL	**482**	**482**	**1384**

Table 14: Summary of Reviewed Biopsy Histology

Biopsy Histology	DECAMP 1	DECAMP 2
Normal Epithelium	349	404
Basal Cell Hyperplasia	58	49
Squamous Metaplasia	18	34
Mild Dysplasia	6	10
Moderate Dysplasia	3	8
Denuded epithelium	127	187
TOTAL	**561**	**692**

Key Research Accomplishments:

Publications:
Silvestri, G. A., et al. (2015). A Bronchial Genomic Classifier for the Diagnostic Evaluation of Lung Cancer. *N Engl J Med,* 373, 243-51.

Oral Presentations:
Billatos, E., Muse, M., Jiwani, A., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning, R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M., Parrish, J.S., Reid, M., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D., Wistuba, I.I., Schnall, M., Vachani, A., Spira, A. (2016, May). *Diagnostic Evaluation of the Indeterminate Pulmonary Nodule Among Military and Veteran Personnel with Suspect Lung Cancer: The DECAMP Consortium.* Presented at the American Thoracic Society Annual Meeting, San Francisco, CA.

Poster Presentations:
Stevenson, C., Billatos, B., Beane-Ebel, J., Campbell, J., Lel, J., Zhang, J., Lenburg, M., Moy, C., Lorenzi, M., Wiegand, B.C., Spira, A.; On behalf of the DECAMP Consortium. (2017, August). *Airway Gene Expression Signatures for the Early Detection and Interception of Lung Cancer via the DECAMP Cohort*. Presented at the 2017 Johnson and Johnson Symposium, Los Angeles, CA.

Wilkerson, M., Campbell, J., Dalgard, C.L., Billatos, E., Pollard, H.B., Browning, R., Stevenson, C., DECAMP Consortium, Spira, A. (2017, August). *RNA sequencing of the bronchial airway identifies molecular subtypes of COPD within the DECAMP consortium.* Presented at the 2017 Military Health System Research Symposium, Kissimmee, FL.

Radin, G., Billatos, E., Snyder, B., Stevenson, C., Duan, F., Gatsonis, C., O'Connor, G., Lenburg, M., Washko, G., Spira, A. (2017, May). *Characterizing clinical and imaging phenotypes of COPD within the DECAMP consortium*. Presented at the American Thoracic Society Annual Meeting, Washington, DC.

Billatos, E., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning, R., Garshick, E., Goldstein, R.H., Vachani, A., Keith, R.L., More, K., Morris, M., Parrish, J.S., Reid, M., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P, Remick, D., Wistuba, I.I., Schnall, M., Spira, A. (2016, October). *Diagnostic Evaluation of the Indeterminate Pulmonary Nodule Among Military and Veteran Personnel with Suspect Lung Cancer: The DECAMP Consortium*. Presented at Evans Day, Boston University, Boston, MA.

Jiwani, A. Z., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning Jr., R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M.J., Parrish, J.S., Reid, M., Vachani, A., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D.G., Wistuba, I.I., Schnall, M., and Spira, A. (2015, May).
Detection and validation of molecular biomarkers for the early detection of lung cancer among military and veteran populations: The DECAMP consortium. Presented at the American Thoracic Society Conference, Denver, Colorado.

Jiwani, A. Z., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning Jr., R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M.J., Parrish, J.S., Reid, M., Vachani, A., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D.G., Wistuba, I.I., Schnall, M., and Spira, A. (2014, October). *Airway gene-expression in the DECAMP consortium as a molecular window into COPD and lung cancer.* Presented at American Association of Bronchology and Interventional Pulmonology Research Symposium, Austin, TX.

Jiwani, A. Z., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning Jr., R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M.J., Parrish, J.S., Reid, M., Vachani, A., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D.G., Wistuba, I.I., Schnall, M., and Spira, A. (2014, October). *Detection and validation of molecular biomarkers for the early detection of lung cancer among military and veteran populations: The DECAMP consortium.* Presented at American College of Chest Physicians Conference, Austin, TX.

Reportable Outcomes:
n/a

Conclusion:

Overall, we have made significant progress towards the goals of this consortium over the past 12 months. We have continued to make strides in enrollment and adjudication, including the addition of two new recruitment sites, and have maintained consistent meetings between the numerous cores and working groups within the consortium. We have also identified and addressed needs in leadership in order to continue to increase our enrollment numbers, ensure that clinical data entry is complete and that the scientific aims of the project are being met. Finally, we have made significant progress in our scientific oncology discovery aims, laying the groundwork for the development of new diagnostic molecular airway biomarkers for lung cancer. We feel confident that this momentum will continue through the 18 month no cost extension, and that our progress in the past 12 months in securing additional funding for the consortium will ensure its continued impact.